Remarks

Claims 1 to 48 are pending in the present patent application. Claims 7 to 19, 21 to 32 and 34 to 48 have been withdrawn as directed to non-elected subject matter.

Request for Reconsideration of the Further Restriction Requirement

The Action of October 25, 2005 ("First Action") required applicants to select one of the following three groups of allegedly patentably distinct inventions for examination (First Action at 2).

I. Claims 1 to 6, 20 and 33, drawn to a compound of formula (I), a composition comprising a compound of formula (I) and a diagnostic agent comprising a compound of formula (I);

II. Claims 7 to 19, 21 to 32 and 34 to 47, drawn to a method for use of a compound of formula (I); and

III. Claim 48, drawn to a process for preparing a compound of formula (I).

In response, Applications filed a Reply on November 22, 2005 ("Reply") that elected the claims of Group I for prosecution and reserved the right to rejoin the claims of Group II in accordance with MPEP § 821.04. Applicants also elected the species guanidocarbonyl-1-(7-methyl-7H-pyrrolo[2,3-d]pyrimidin-4-yl-1H-indole hydrochloride. *Id.*

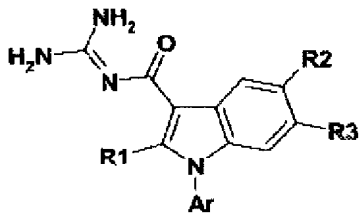
Apparently based upon Applicants' species election, the Action now further restricts claims 1 to 6, 20 and 33 to compounds of formula I as defined in claim 1 wherein Ar is 7H-pyrrolo-[2,3-d]pyrimidin-4-yl (Action at 2 to 4). Applicants submit respectfully that this further restriction requirement is improper because it divides Applicants' Markush claim in contravention to the requirements of MPEP §803.02 and the case law.

A. MPEP §803.02 Considerations

MPEP §803.02 provides that there is no basis for a restriction of a Markush claimed invention where two factors are met, *i.e.*,

> … compounds included within a Markush group (1) share a common utility and (2) share a substantial structural feature …

Applicants' claimed invention meets the aforesaid factors. That is: (A) the compounds of the claimed invention all share a substantial structural feature, *i.e.*, the compound of the formula I



(I)

; and B) the compounds share a common utility, *i.e.*, being useful for the treatment of diseases caused by ischemia and by reperfusion. Indeed, the Action has based its further restriction requirement soley on the constituents of the Markush group "Ar" – all other variables remain the same.

Moreover, it is well-established that the Action must provide reasons and/or examples to support conclusions when issuing a restriction requirement. MPEP § 803. Applicants respectfully submit, however, that the Action has not met this requirement. The Action has based its conclusion on a presumption, the truth of which has not been shown. In this regard, the Action presumes that the constituents of the Markush group substituents are so dissimilar that the chemical compounds within the scope of the defined substituents do not function similarly (Action at 3 to 4). The Action, however, provides no evidence or scientific reasoning to support its "presumption." Accordingly, Applicants respectfully submit that the further restriction requirement is improper on its face for failing to comply with the requirements set forth in the MPEP.

B. Case Law Considerations

As detailed below, well-settled case law such as, for example, *In re Harnisch*, 206 U.S.P.Q. 300 (CCPA 1980) and *Ex parte Dahlen and Zwilgmeyer,*42 U.S.P.Q. 208 (Bd. App., 1938), supports Applicants' position that the present restriction requirement is improper because, as stated above, the Action has provided ***no*** evidence or technical reasoning to support its apparent conclusion that the compounds of formula I do ***not*** share a common utility and do ***not*** share a substantial structural feature.

In *In re Harnisch*, 206 U.S.P.Q. 300 (CCPA 1980), the court found that an invention claimed in a Markush type claim was proper for compounds having a common utility and "***a single structural similarity***" (emphasis added). In particular, in agreeing with its earlier decisions, the court stated that a Markush group was proper where there is a

> grouping of compounds having the ***same nuclei but side chains wherein there was a wide variation*** ... and had ***a community of properties justifying their grouping*** ... was not repugnant to principles of scientific classification.

In re Harnisch, 206 U.S.P.Q. at 305 (emphasis added). The Court held that, when such criteria exist, there is unity of invention within the claimed Markush group. *Id.*

Applicants' claimed invention meets the standard of *In re Harnisch* as it indeed has the requisite single structural similarity (*i.e.*, the substantial structural feature from MPEP §803.02) and shares a common utility, as noted above. Therefore, there is no propriety for the present further restriction requirement. Accordingly, reconsideration and withdrawal of the further restriction requirement is requested respectfully.

Discussion of the Objection

Claims 1 to 6, 20 and 33 are objected to as containing non-elected subject matter (Action at 4). Applicants respectfully request that this rejection be deferred pending resolution of the further restriction requirement.

Discussion of the Rejection under 35 U.S.C. § 103(a)

The non-elected subject matter of claims 1, 2, 5, 6, 20 and 33 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over U.S. Patent No. 5,852,046 to Lang et al. ("Lang") (Action at 7). Applicants respectfully traverse this rejection as the Action fails to provide any motivation as to why a person of ordinary skill in the art having Lang before him at the time of the present invention would have been motivated to modify its teaching in such a way as to obtain any compound of the present invention.

Applicants' claimed invention defines indole derivatives substituted at the 3 position by guanidyl and substituted at N by substituent Ar, which, in turn, comprises an N-bicycloheteroaryl moiety. Lang, however, discloses generally 2-guanidyl substituted heterocyclic compounds, including indoles, which are further substituted at the N by optionally substituted alkyl(C_3-C_{10})-cycloalkyl (*see* col. 1, lines 17 to 67 and col. 2, lines 1 to 11). In particular, Lang discloses indole substituted by optionally substituted alkyl (C_3-C_{10})-cycloalkyl where Y is NR(7), R(7) is R(8)-C_nH_{2n}-, and R(8) is optionally substituted (C_3-C_{10}) cycloalkyl (id.). Lang thus ***does not*** disclose either the guanidyl substitution at position 3 or the N-bicycloheteroaryl substituent of the presently claimed indole derivatives. Thus, Lang does not disclose compounds which generically overlap those of the present invention.

Moreoever, Lang ***does not*** contain any teaching that would motivate one of ordinary skill in the art to modify its disclosure in a way that would produce a claimed compound. To establish a *prima facie* case of obviousness "there must be some teaching, suggestion or motivation in the prior art to make the specific combination that was made by the applicant." *In re Dance*, 160 F.3d 1339, 1343, 48 USPQ2d 1635, 1637 (Fed. Cir. 1998). "In other words, the examiner must show reasons that the skilled artisan, confronted with the same problem as the inventor and with no knowledge of the claimed invention, would select the elements from the

cited prior art references for combination in the manner claimed." *In re Rouffet*, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1458 (Fed. Cir. 1998).

The Action appears to link the alleged structural similarity of the compounds of Applicants' claimed invention to those disclosed in Lang in an attempt to establish that claims 1, 2, 5, 6, 20 and 33 are obvious (Action at 8). As explained above, the difference between Applicants' claimed compounds and those of Lang is that Lang does not teach or suggest the presently claimed 3-guanidyl and N-bicycloheteroaryl substituted indole derivatives of the present invention.

Significantly, however, the Action has not established, as it must, any rationale for why one of ordinary skill in the art would have been motivated to modify the teachings of Lang to substitute the indole derivatives disclosed therein with a guanidyl substituent on position 3 or an N-bicycloheteroaryl substituent. MPEP § 2143 (to establish a *prima facie* case of obviousness, the Action must demonstrate some suggestion or motivation to modify the reference compound or to combine reference teachings). To the extent that ***any*** rationale was given in the Action, that rational was directed to the alleged expectation of treating conditions such as atherosclerosis based on the alleged structural similarity of the compounds of Lang and ***not*** for modifying such compounds as are presently claimed. Indeed, Lang ***does not disclose*** N-bicycloheteroaryl substituents or, for example, whether particular benefits would result from such a substituent.

Moreover, although it would have been theoretically ***possible*** to modify Lang in a way that would have produced the claimed invention, much more is required of a reference that is applied in the context of § 103. The mere ***possibility*** that the prior art can be modified or improved does not itself provide the requisite motivation to do so. *In re Dien*, 152 U.S.P.Q. 550 (C.C.P.A. 1967) (incentive to seek improvement of existing process held to not render change made by applicant obvious, even where the change was one capable of being made from theoretical point of view). The mere ***possibility*** for modification and improvement is not the

"motivating force" that the Board and the Federal Circuit have invariably required. If it were, then no modification would ever lack motivation since ***some*** change is always possible. It is only with the improper use of hindsight and with the benefit of the Applicants' disclosure that one can discern the desirability of the claimed inventions.

Absent the identification of a rationale to modify the compounds of Lang (as is the case here), a *prima facie* case of obviousness cannot be supported for claims 1, 2, 5, 6, 20 and 33. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Discussion of the Double Patenting Rejection

Claims 1, 2, 5, 6, 20 and 33 are provisionally rejected under the judicially created doctrine of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1, 2, 6, 7, 21 and 34 of U.S. patent application Serial No. 10/749,630 to Kleeman et al. ("Kleeman") (Action at 12 to 13). Applicants request that this rejection be deferred pending some identification of allowable subject matter, as it likely can be readily resolved (depending upon the subject matter ultimately allowed) through the filing of a suitable terminal disclaimer.

Conclusion

Applicants respectfully submit that this application is now in condition for allowance. Accordingly, an indication of allowability and an early Notice of Allowance are respectfully requested. If there are any issues that can be resolved by a telephone conference or an Examiner's amendment, the Examiner is invited to call the undersigned attorney at (908) 231-3410.

The Commissioner is hereby authorized to charge the fee required and any additional fees that may be needed to Deposit Account No. **18-1982** in the name of Aventis Pharmaceuticals Inc.

Respectfully submitted,

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